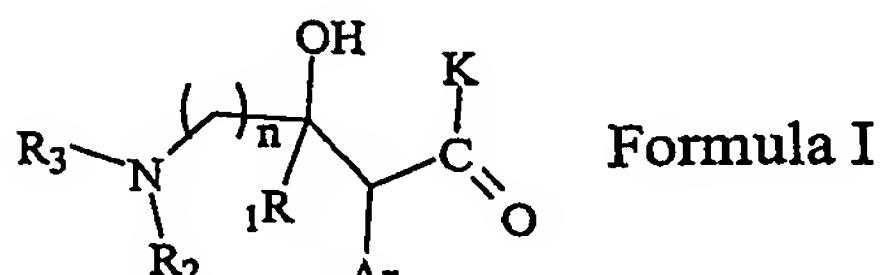


WE CLAIM:

1. A complex comprising a compound of one of formula I - VIII, XII or XIII, in association with an adrenomedullin (AM) peptide, wherein formulas I - VIII, XII and XIII are:

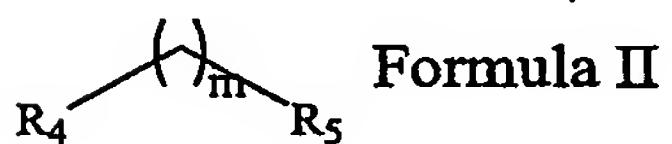


wherein:

5 K is OR_{32} , SR_{32} , or $NR_{33}R_{34}$ where R_{32} is H or lower alkyl, and R_{33} and R_{34} are the same or different and each is selected from H and lower alkyl;
Ar is aryl optionally substituted aryl optionally substituted with one or more groups selected from -OH, -NH₂, -SH, halogen and hydrocarbyl;
n is an integer from 1-3; and

10 R₁, R₂ and R₃ are the same or different and is each selected from H, hydrocarbyl and a heterocyclic ring; or
R₁ and R₂ together form a heterocyclic ring including the intervening nitrogen, and R₃ is selected from H, hydrocarbyl and a heterocyclic ring; or
R₁ is selected from H or hydrocarbyl and R₂ and R₃ together form a heterocyclic ring including the intervening nitrogen;

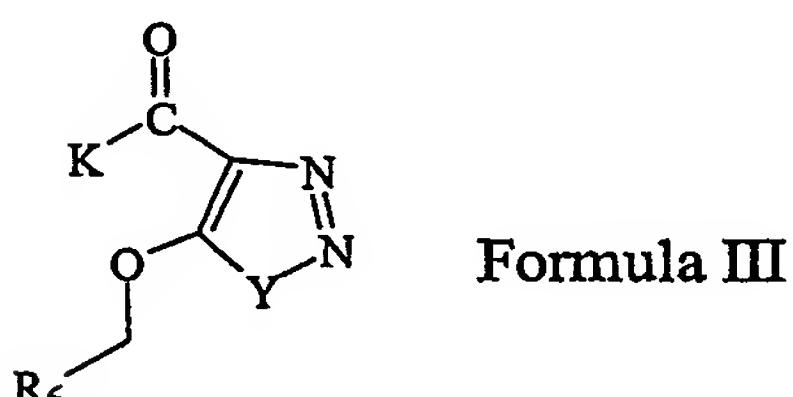
15



wherein:

R_4 and R_5 may be the same or different and each is an aryl group substituted with $-C(O)K$, and optionally further substituted with one or more groups selected from $-OH$, $-NH_2$, $-SH$, halogen, hydrocarbyl and a heterocyclic ring, where K is as defined above; and

20 m is an integer from 1-3;



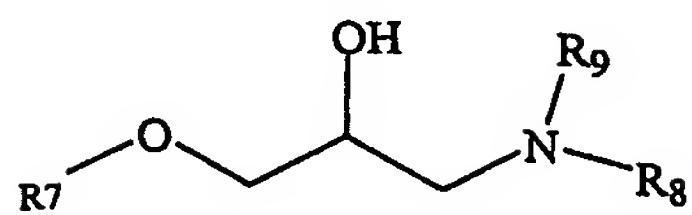
wherein:

K is as defined above;

Y is selected from CH₂, O, S and NH; and

R_6 is aryl optionally substituted with one or more groups selected from -OH, -NH₂, -SH,

25 halogen, hydrocarbyl and a heterocyclic ring;



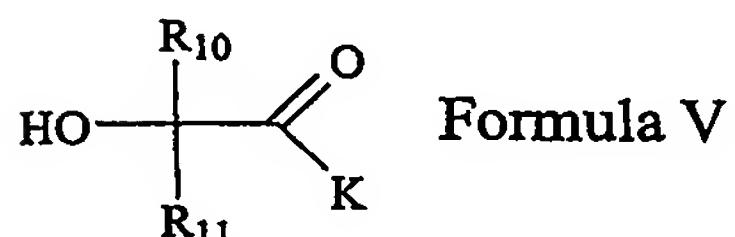
Formula IV

wherein:

R₇ is aryl optionally substituted with one or more groups selected from -OH, -NH₂, -SH, halogen, a heterocyclic ring and hydrocarbyl; and

R₈ and R₉ are the same or different and are each hydrocarbyl, optionally substituted with one or more halogens or lower alkyl groups, or

R₈ and R₉ together form a heterocyclic ring having five, six or seven atoms, including the intervening nitrogen and optionally containing other heteroatoms, and also optionally substituted with one or more halogens or lower alkyl groups;

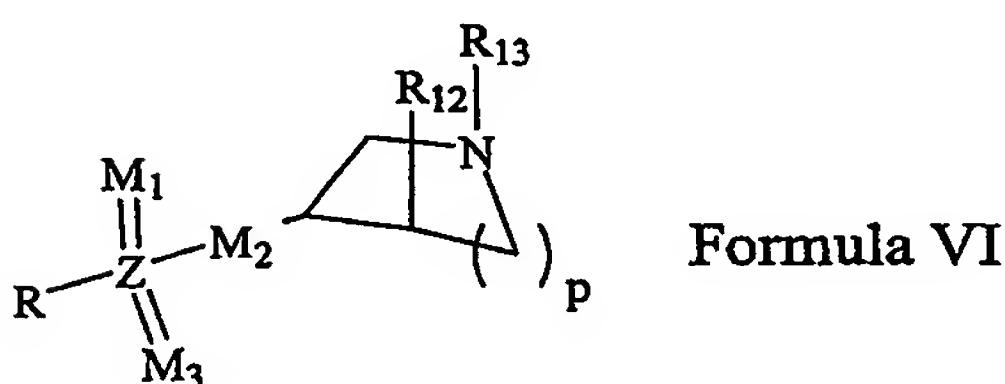


Formula V

wherein:

10 K is as defined above; and

R₁₀ and R₁₁ are the same or different and each is an aryl group, optionally substituted with a second aryl group that may be the same or different and the aryl groups may be substituted with one or more groups selected from -OH, -NH₂, -SH, halogen, a heterocyclic ring and hydrocarbyl;



Formula VI

wherein:

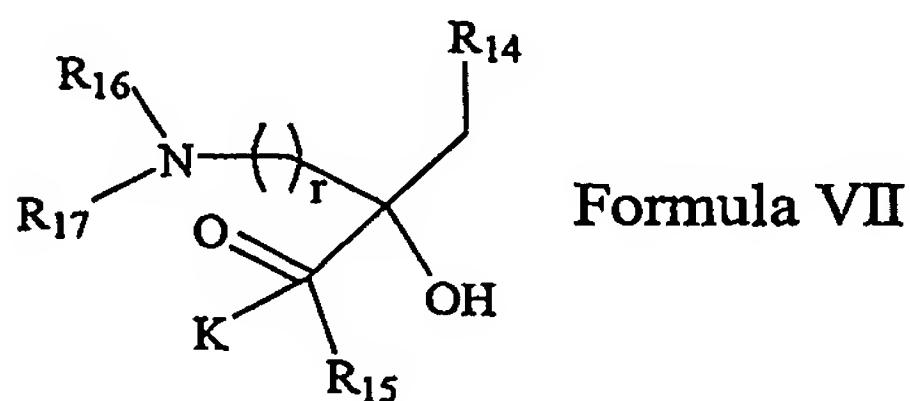
15 p is an integer from 1-3;

M₁, M₂, and M₃ are the same or different and each is S or O;

Z is S, C or P;

R is hydrocarbyl or OR₃₅, where R₃₅ is H or hydrocarbyl; and

20 R₁₂ and R₁₃ are the same or different and each is hydrocarbyl, a heterocyclic ring or lower alkyl, or R₁₂ and R₁₃ together form a ring;



Formula VII

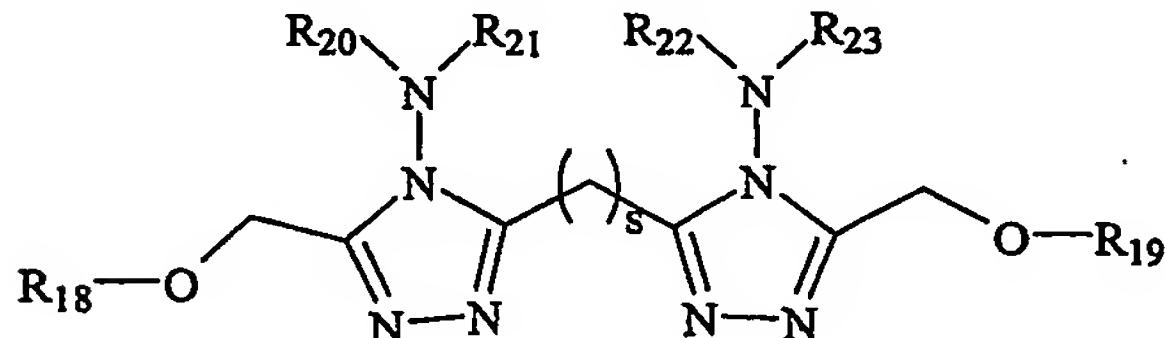
wherein:

K is as defined above;

r is an integer from 1-3;

R₁₄ and R₁₅ are the same or different and each is aryl optionally substituted with one or more groups selected from -OH, -NH₂, -SH, halogen, a heterocyclic ring and hydrocarbyl; and

5 R₁₆ and R₁₇ are the same or different and each is hydrocarbyl or a heterocyclic ring;



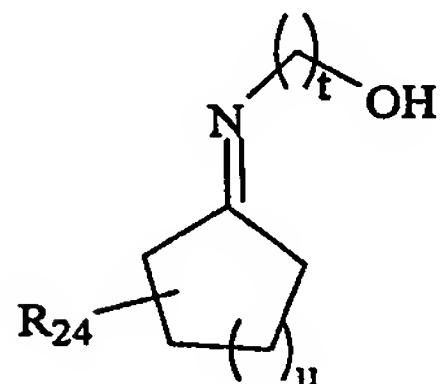
Formula VIII

wherein:

s is an integer from 1-10;

R₂₀, R₂₁, R₂₂ and R₂₃ are the same or different and each is H, aryl, optionally substituted with one or more halogen or lower alkyl groups, hydrocarbyl and a heterocyclic ring; and

10 R₁₈, R₁₉ are the same or different and each is aryl optionally substituted with one or more groups selected from -OH, -NH₂, -SH, halogen or lower alkyl;



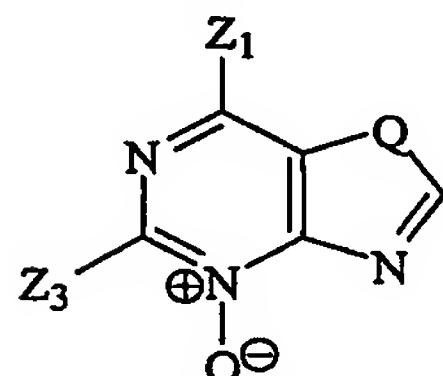
Formula XII

wherein:

t is an integer from 1-5;

u is an integer from 1-2; and

15 R₂₄ is selected from H, a heterocyclic ring and hydrocarbyl, optionally substituted by halogen; and



Formula XIII

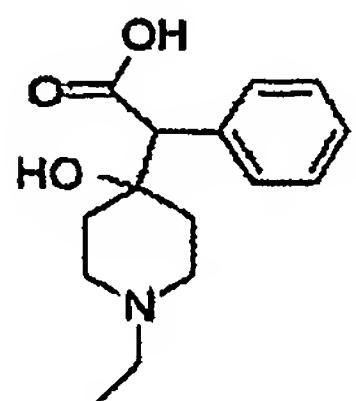
wherein:

Q is selected from CH₂, NH, S and O; and

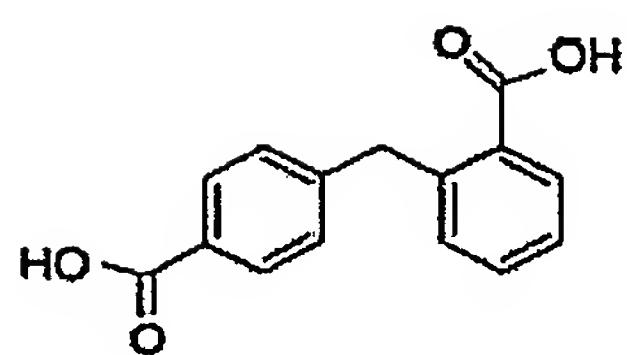
Z₁ and Z₃ are the same or different and selected from CH₃, NH₂, OH and SH.

20 or tautomers thereof.

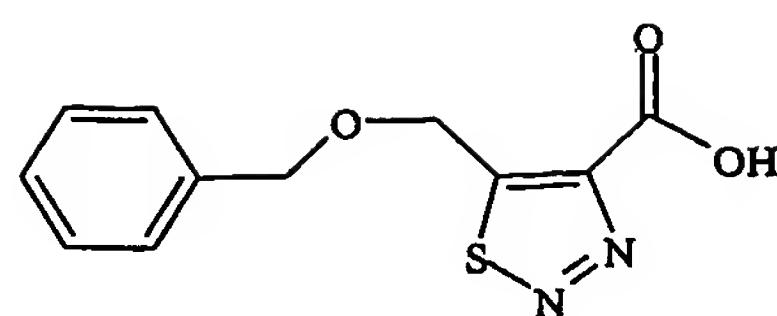
2. The complex of claim 1, wherein the compound is selected from



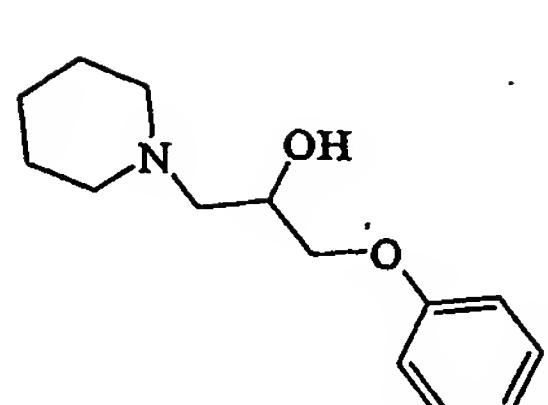
formula I'



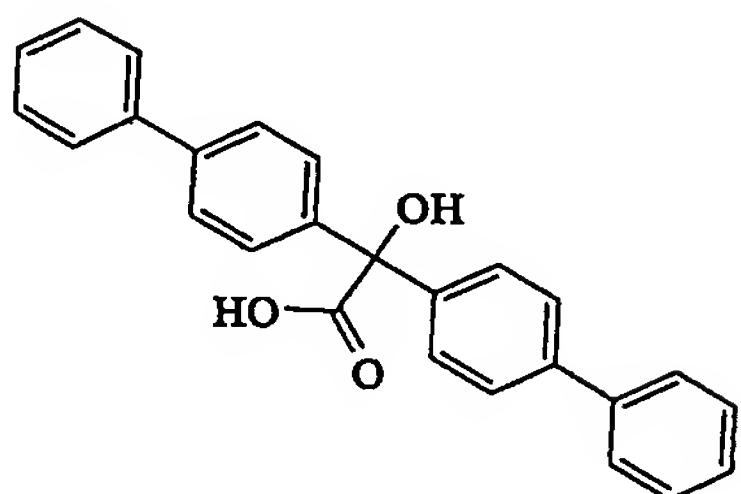
formula II'



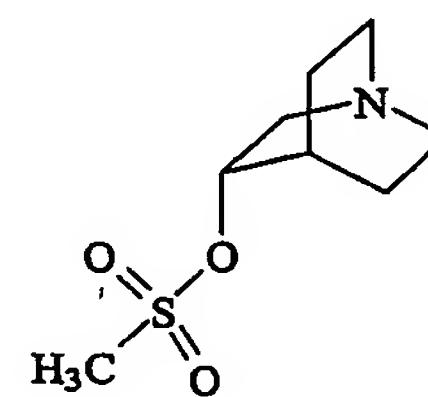
formula III'



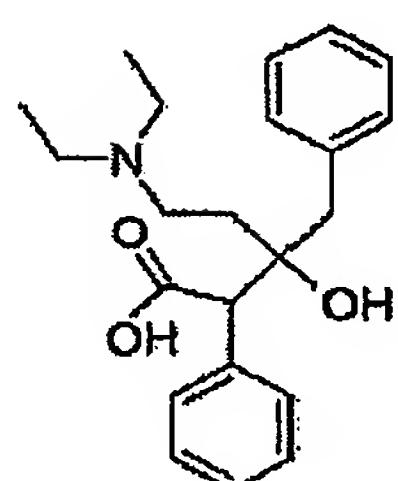
formula IV'



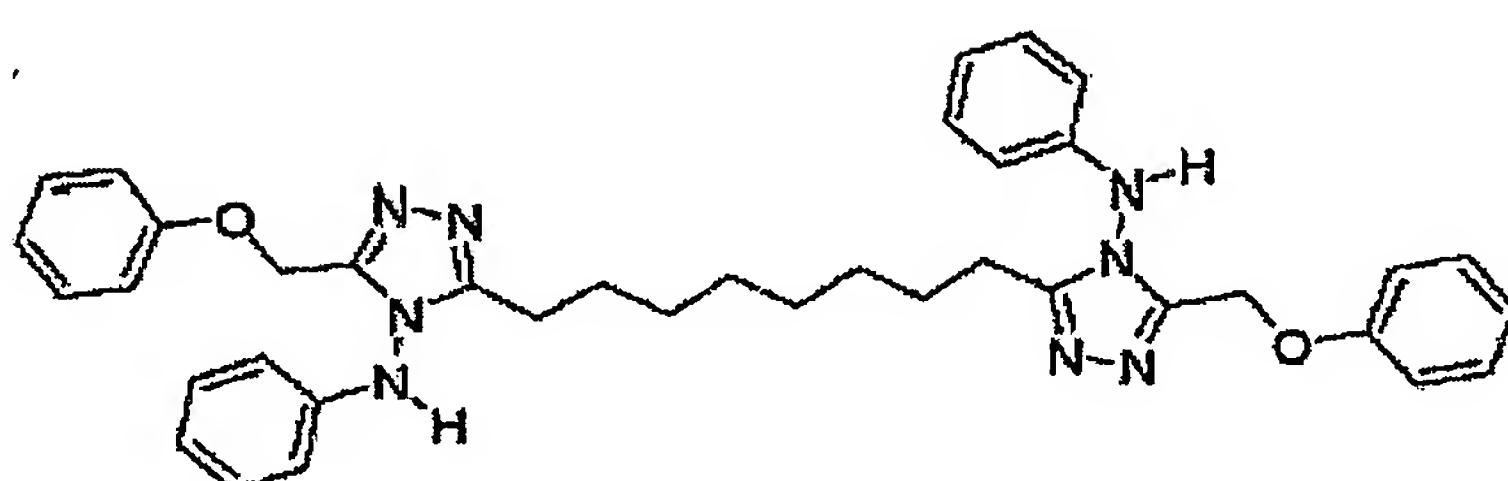
formula V'



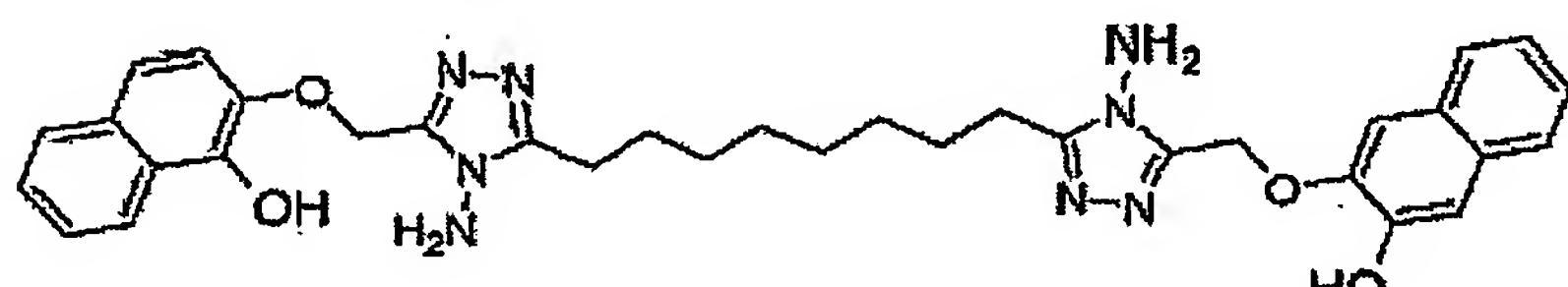
formula VI'



formula VII'

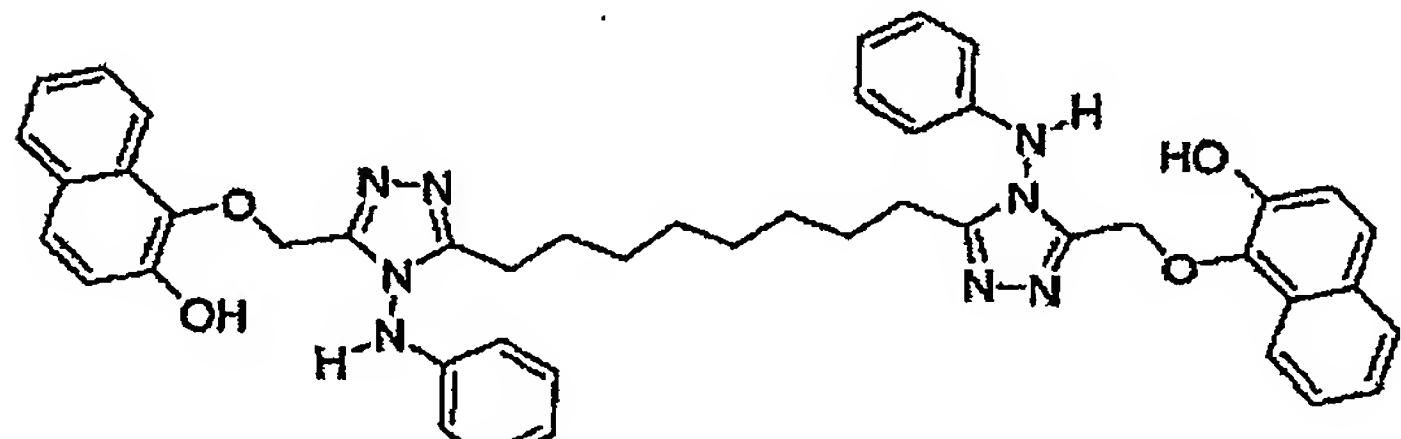


formula VIII'

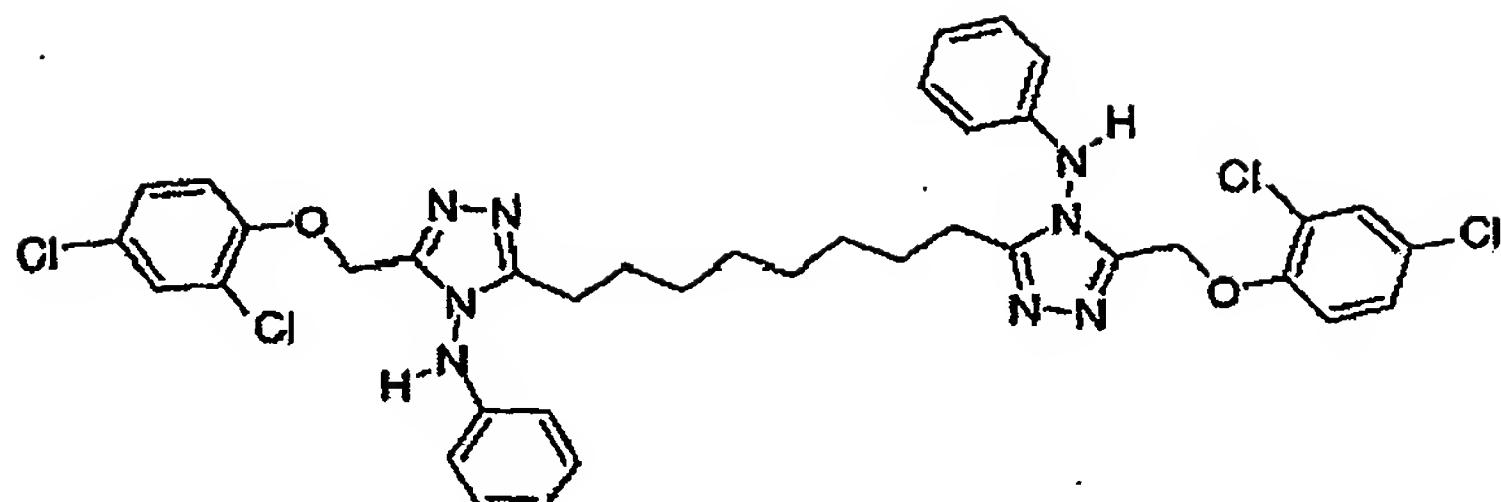


formula IX'

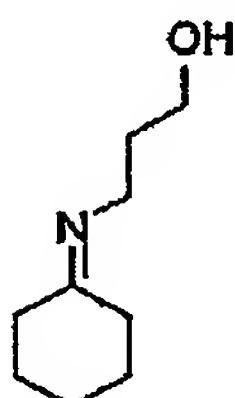
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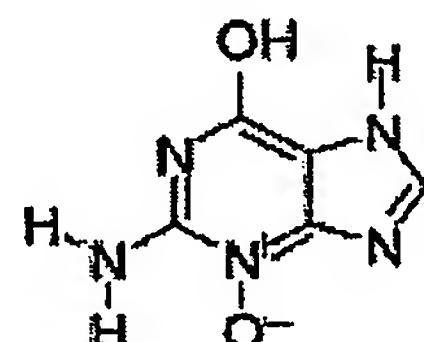
formula X'



formula XI',



formula XII', and



formula XIII',

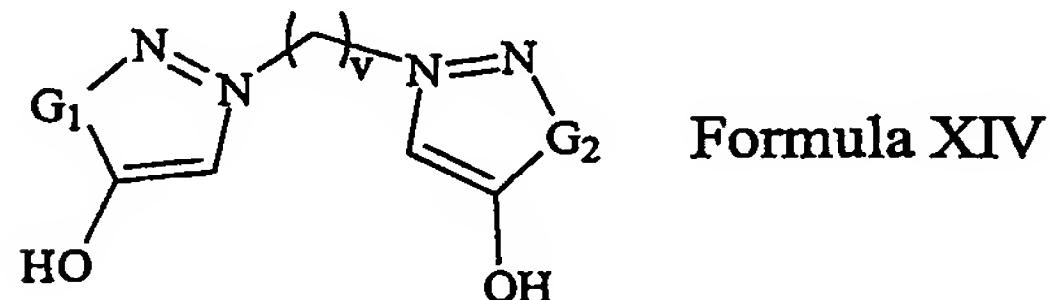
5 or a pharmaceutically acceptable salt thereof.

3. The complex of claim 1, which is in an animal.

4. The complex of claim 1, which is *in vitro*.

10

5. A complex comprising a compound of one of

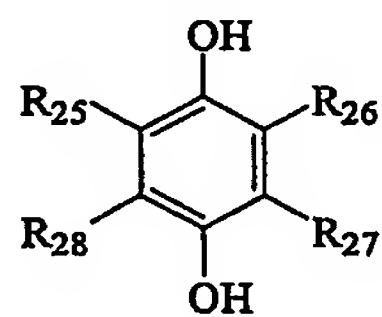


Formula XIV

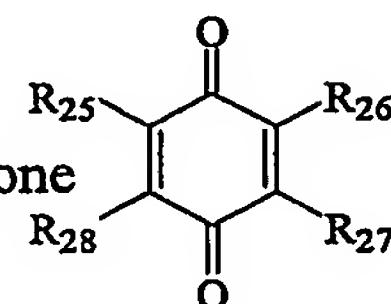
wherein:

v is an integer from 1-3; and

G₁ and G₃ are the same or different and each is selected from CH₂, NH, S and O;



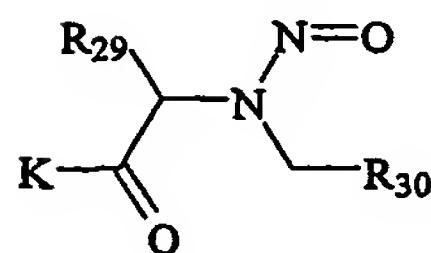
or the corresponding quinone



15 Formula XVI

wherein:

R₂₅, R₂₆, R₂₇, and R₂₈ are the same or different and each is selected from halogen and hydrocarbyl, particularly lower alkyl; and



Formula XVII

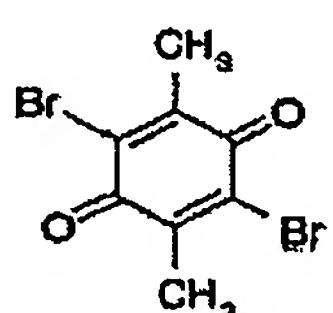
wherein:

K is as defined above, and

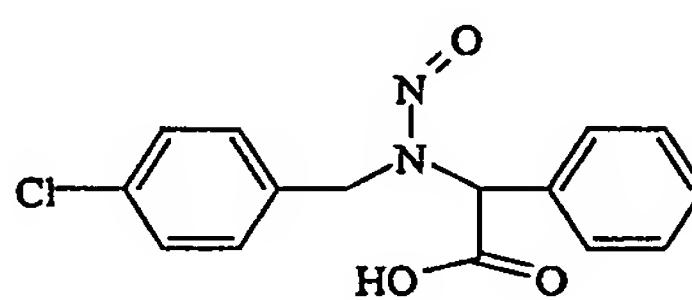
R_{29} and R_{30} are the same or different and each is aryl optionally substituted with one or more groups selected from -OH, -NH₂, -SH, halogen and hydrocarbyl;

5 in association with a gastric releasing peptide (GRP).

6. The complex of claim 4, wherein the compound is of one of



or



Formula XIV',

Formula XVI', or

Formula XVII'.

10 7. The complex of claim 4, which is in an animal (e.g., a mammal).

8. The complex of claim 4, which is *in vitro*.

9. A pharmaceutical composition comprising a compound of one of formula I - VIII, XII - XIV, or XVI - XVII, as defined in claim 1 and a pharmaceutically acceptable carrier.

10. The pharmaceutical composition of claim 9, wherein the compound is of one of formula I' - XIV' or XVI' - XVII', as defined in claim 2.

20 11. A method for inhibiting an activity of an AM peptide, comprising contacting the peptide
with an effective amount of a compound of one of formula I - VII as defined in claim 1.

12. The method of claim 11, wherein the compound is of one of formula I' - VII', as defined in claim 2.

13. The method of claim 11, wherein the peptide and compound are in an animal.
14. The method of claim 11, wherein the peptide and compound are *in vitro*.
- 5 15. The method of claim 11, wherein the activity of the AM peptide is stimulation of the level of intracellular cAMP.
16. The method of claim 11, wherein the activity of the AM peptide is vasodilation.
- 10 17. A method for treating a condition that is mediated by over-expression and/or activity of AM, comprising administering to a patient in need of such treatment an effective amount of a compound of one of formula I – VII, as defined in claim 1.
- 15 18. The method of claim 17, wherein the compound is of one of formula I' - VII', as defined in claim 2.
19. The method of claim 17, wherein the condition is type 2 diabetes or cancer.
- 20 20. A method for stimulating an activity of an AM peptide, comprising contacting the peptide with an effective amount of a compound of one of formula VIII, XII or XIII, as defined in claim 1.
21. The method of claim 20, wherein the compound is of one of formula VIII' - XIII', as defined in claim 2.
- 25 22. The method of claim 20, wherein the peptide and compound are in an animal.
23. The method of claim 20, wherein the peptide and compound are *in vitro*.
- 30 24. The method of claim 20, wherein the activity of the AM peptide is stimulating the level of intracellular cAMP.
25. The method of claim 20, wherein the activity of the AM peptide is vasodilation.

26. A method for treating a condition that is mediated by under-expression and/or activity of AM, comprising administering to a patient in need of such treatment an effective amount of a compound of one of formula VIII, XII or XIII, as defined in claim 1.

5 27. The method of claim 26, wherein the compound is of one of formula VIII' - XIII', as defined in claim 2.

28. The method of claim 26, wherein the condition is renal or cardiovascular disease, sepsis, or central nervous system ischemia.

10

29. A method for inhibiting an activity of a GRP peptide, comprising contacting the peptide with an effective amount of a compound of formula XIV or XVI, as defined in claim 5.

15 30. The method of claim 29, wherein the compound is of formula XIV' or XVI', as defined in claim 6.

31. The method of claim 29, wherein the peptide and compound are in an animal.

32. The method of claim 29, wherein the peptide and compound are *in vitro*.

20

33. The method of claim 29, wherein the activity of the GRP peptide is the stimulation of intracellular IP₃ or Ca⁺².

25 34. The method of claim 29, wherein the activity of GRP is stimulating angiogenesis, suppressing food intake, regulating glucose homeostasis, or stimulating hypotension.

35. A method for treating a condition that is mediated by over-expression and/or activity of GRP, comprising administering to a patient in need of such treatment an effective amount of a compound of formula XIV or XVI, as defined in claim 5.

30

36. The method of claim 35, wherein the compound is of formula XIV' or XVI', as defined in claim 6.

37. The method of claim 35, which is a method for inhibiting or reducing tumor growth, treating low blood pressure or an eating disorder, or improving breathing in a premature baby.

5 38. A method for stimulating an activity of a GRP peptide, comprising contacting the peptide with an effective amount of a compound of formula XVII, as defined in claim 5.

39. The method of claim 38, wherein the compound is of formula XVII', as defined in claim 6.

10 40. The method of claim 38, wherein the peptide and compound are in an animal.

41. The method of claim 38, wherein the peptide and compound are *in vitro*.

15 42. The method of claim 38, wherein the activity of the GRP peptide is the stimulation of intracellular IP₃ or Ca⁺².

43. The method of claim 38, wherein the activity of GRP is stimulating angiogenesis, suppressing food intake, regulating glucose homeostasis, or stimulating hypotension.

20 44. A method for treating a condition that is mediated by under-expression and/or activity of GRP, and/or that would benefit from increased expression of GRP comprising administering to a patient in need of such treatment an effective amount of a compound of formula XVII, as defined in claim 5.

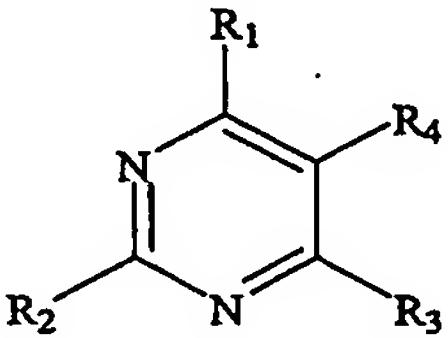
25 45. The method of claim 44, wherein the compound is of formula XVII', as defined in claim 6.

46. The method of claim 44, wherein the condition is obesity, diabetes, hypertension, coronary or peripheral artery disease, tissue ischemia, organ or tissue transplantation, or acceleration or enhancing of fracture repair or wound healing.

30 47. A method for detecting an AM peptide, comprising
contacting a sample suspected of containing the peptide with one or more detectably labeled compounds of formula I through VIII, or formula XII through XIII, as defined in claim 1, and
detecting labeled compound that is associated with the peptide.

48. The method of claim 38, wherein the detectably labeled compound is of formula I' - XIII', as defined in claim 2.

5 49. A method for detecting a GRP peptide, comprising
contacting a sample suspected of comprising the peptide with one or more detectably
labeled compounds of formula XIV, XVI or XVII, as defined in claim 5 or


Formula XV
wherein

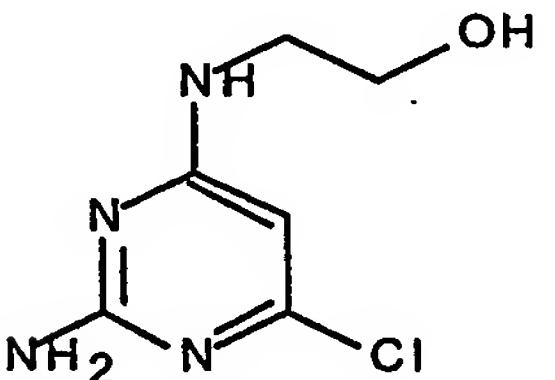
R₁ is: -R₅-(CH₂)_n-CH(R₆)OH, and R₅ is NH, S or O, R₆ is H or CH₃; and n is an integer from 1-
10 4;

R₂ is NH₂, substituted amino or acetamide;

R₃ is H, halogen, CH₃, or CF₃; and

R₄ is H, alkyl, substituted alkyl, alkenyl, alkoxy or halogen; and
detecting labeled compound that is associated with the peptide.

15 50. The method of claim 49, wherein the detectably labeled compound is selected from formula
XIV', XVI' or XVII', as defined in claim 6 or


formula XV'.

20 51. The method of claim 47 or 49, which is performed *in vivo*.

52. The method of claim 47 or 49, which is performed *in vitro*.

53. A kit suitable for treating a subject suffering from a condition mediated by aberrant
25 expression and/or activity of adrenomedullin (AM), comprising one or more compounds of
formula I - VIII, XII or XIII, as defined in claim 1, or a pharmaceutical composition comprising

said compound(s) and a pharmaceutically acceptable carrier, and, optionally, a container or packaging material.

54. The kit of claim 53, wherein the compound(s) is selected from formula I' through XIII', as
5 defined in claim 2.

55. A kit suitable for treating a subject suffering from a condition mediated by an aberrant expression and/or activity of gastrin releasing peptide (GRP), comprising one or more of the compounds of formula XIV, XVI or XVII, as defined in claim 5, or a pharmaceutical
10 composition comprising said compound(s) and a pharmaceutically acceptable carrier, and, optionally, a container or packaging material.

56. The kit of claim 55, wherein the compound(s) is of one of formula XIV', XVI' and/or XVII', as defined in claim 6.

15 57. A kit suitable for detecting an AM peptide, comprising
a) one or more compounds selected from formula I - VIII, XII or XIII, as defined in
claim 1, which is detectably labeled, and, optionally,
b) means to detect the labeled compound associated with (bound to) the peptide.

20 58. The kit of claim 57, wherein the compound(s) is of one of formula I' - XIII', as defined in
claim 2.

59. A kit suitable for detecting a GRP peptide, comprising
a) one or more compounds selected from formula XIV, XVI, XVII, as defined in claim 5
and XV, as defined in claim 49, which is detectably labeled, and, optionally,
b) means to detect the labeled compound associated with (bound to) the peptide.

60. The kit of claim 45, wherein the compound(s) is selected from formula XIV', XVI', XVII', as
30 defined in claim 6 and XV', as defined in claim 50.

61. A kit of claim 53 or 55, which is suitable *in vivo* detection, further wherein said compound is
in a pharmaceutically acceptable carrier.

62. A method for inhibiting GRP-mediated angiogenesis in a subject in need of such treatment, comprising administering to the subject an effective amount of an agent that inhibits GRP, provided that the GRP-mediated angiogenesis is not angiogenesis involved in tumor growth or metastasis.

5

63. A method for preventing or treating condition mediated by GRP-mediated angiogenesis in a subject in need of such treatment, comprising administering to the subject an effective amount of an agent that inhibits GRP, provided that the condition is not angiogenesis dependent tumor growth.

10

64. A method for preventing or treating one of the following angiogenesis-mediated conditions in a subject:

arthritis (*e.g.*, rheumatoid arthritis),

psoriasis,

15 benign growths caused by rapidly dividing cells (*e.g.*, noncancerous melanomas),

brain ischaemia,

vascular diseases,

ocular diseases involving ocular neovascularization or related ocular diseases and disorders,

20 fibrosis,

deep venous thrombosis,

endometriosis, or

wrinkles,

comprising administering to the subject an effective amount of an agent that inhibits

25 GRP.

65. A method for inhibiting angiogenesis-mediated tumor growth in a subject in need of such treatment, comprising

30 administering to the subject an effective amount of an agent that inhibits GRP, and

detecting or monitoring the reduction in blood vessels (inhibition of angiogenesis).

66. The method of claim 62, wherein the agent is a compound of formula XV as defined in claim 49.

67. The method of claim 63, wherein the agent is a compound of formula XV as defined in
claim 49.

68. The method of claim 64, wherein the agent is a compound of formula XV as defined in
5 claim 49.

69. The method of claim 65, wherein the agent is a compound of formula XV as defined in
claim 49.

10 70. The method of claim 62, wherein the agent is a compound of formula XV' as defined in
claim 50.

71. The method of claim 63, wherein the agent is a compound of formula XV' as defined in
15 claim 50.

72. The method of claim 64, wherein the agent is a compound of formula XV' as defined in
claim 50.

73. The method of claim 65, wherein the agent is a compound of formula XV' as defined in
20 claim 50.

74. A method for treating low blood pressure or an eating disorder in a subject in need of such
treatment, comprising administering to the subject an effective amount of a compound of
formula XV as defined in claim 49.

75. The method of claim 74, wherein the compound is of formula XV' as defined in claim 50.